CLAIMS

The subject matter claimed is:

1. A method for making a composition for obtaining enhanced mucosal absorption of heparin comprising:

(a) dissolving an amphiphilic heparin derivative comprising heparin covalently bonded to a hydrophobic agent selected from the group consisting of bile acids, sterols, alkanoic acids, and mixtures thereof in a water phase;

(b) dispersing the water phase containing the dissolved amphiphilic heparin derivative in an organic phase such that an emulsion is formed; and

(c) drying the emulsion to result in the composition.

2. The method of claim 1 wherein said hydrophobic agent is a bile acid selected from the group consisting of cholic acid, deoxycholic acid, chenodeoxycholic acid, lithocholic acid, ursocholic acid, ursodeoxycholic acid, isoursodeoxycholic acid, lagodeoxycholic acid, glycocholic acid, taurocholic acid, glycodeoxycholic acid, glycochenodeoxycholic acid, dehydrocholic acid, hyocholic acid, hyodeoxycholic acid, and mixtures thereof.

3. The method of claim 2 wherein said bile acid is deoxycholic acid.

4. The method of claim 1 wherein said hydrophobic agent is a sterol selected from the group consisting of cholestanol, coprostanol, cholesterol, epicholesterol, ergosterol, ergocalciferol, and mixtures thereof.

5. The method of claim 1 wherein said hydrophobic agent is an alkanoic acid comprising about 4 to 20 carbon atoms.

6. The method of claim 5 wherein said alkanoic acid is a member selected from the group consisting of butyric acid, valeric acid, caproic acid, caprylic acid, capric acid, lauric acid, myristic acid, palmitic acid, stearic acid, and mixtures thereof.

7. The method of claim 1 wherein said heparin is a member selected from the group consisting of low molecular weight heparin, high molecular weight heparin, heparin fragments, recombinant heparin, heparin analogs, polysaccharides containing heparin activity, and mixtures thereof.

8. A method for making a composition for obtaining enhanced mucosal absorption of heparin comprising dispersing an amphiphilic heparin derivative comprising heparin covalently bonded to a hydrophobic agent selected from the group consisting of bile acids, sterols, alkanoic acids, and mixtures thereof in an oil phase.

9. The method of claim 8 wherein said hydrophobic agent is a bile acid selected from the group consisting of cholic acid, deoxycholic acid, chenodeoxycholic acid, lithocholic acid, ursocholic acid, ursodeoxycholic acid, isoursodeoxycholic acid, lagodeoxycholic acid, glycocholic acid, taurocholic acid, glycodeoxycholic acid, glycochenodeoxycholic acid, dehydrocholic acid, hyocholic acid, hyodeoxycholic acid, and mixtures thereof.

10. The method of claim 9 wherein said bile acid is deoxycholic acid.

11. The method of claim 8 wherein said hydrophobic agent is a sterol selected from the group consisting of cholestanol, coprostanol, cholesterol, epicholesterol, ergosterol, ergocalciferol, and mixtures thereof.

12. The method of claim 8 wherein said hydrophobic agent is an alkanoic acid comprising about 4 to 20 carbon atoms.

13. The method of claim 12 wherein said alkanoic acid is a member selected from the group consisting of butyric acid, valeric acid, caproic acid, caprylic acid, capric acid, lauric acid, myristic acid, palmitic acid, stearic acid, and mixtures thereof.

14. The method of claim 8 wherein said heparin is a member selected from the group consisting of low molecular weight heparin, high molecular weight heparin, heparin fragments, recombinant heparin, heparin analogs, polysaccharides containing heparin activity, and mixtures thereof.

15. The method of claim 8 wherein said oil phase is a pharmaceutically acceptable oil.

16. A method for making a composition for obtaining enhanced mucosal absorption of heparin comprising:

(a) dissolving an amphiphilic heparin derivative comprising heparin covalently bonded to a hydrophobic agent selected from the group consisting of bile acids, sterols, alkanoic acids, and mixtures thereof in water or a water/organic co-solvent;

(b) dispersing the water or water/organic co-solvent containing the dissolved amphiphilic heparin derivative in an oil phase; and

(c) evaporating the water or water/organic co-solvent, resulting in the amphiphilic heparin derivative dispersed in the oil phase.

17. The method of claim 16 wherein said hydrophobic agent is a bile acid selected from the group consisting of cholic acid, deoxycholic acid, chenodeoxycholic acid, lithocholic acid, ursocholic acid, ursodeoxycholic acid, isoursodeoxycholic acid, lagodeoxycholic acid, glycocholic acid, taurocholic acid, glycodeoxycholic acid, glycochenodeoxycholic acid, dehydrocholic acid, hyocholic acid, hyodeoxycholic acid, and mixtures thereof.

18. The method of claim 17 wherein said bile acid is deoxycholic acid.

19. The method of claim 16 wherein said hydrophobic agent is a sterol selected from the group consisting of cholestanol, coprostanol, cholesterol, epicholesterol, ergosterol, ergocalciferol, and mixtures thereof.

20. The method of claim 16 wherein said hydrophobic agent is an alkanoic acid comprising about 4 to 20 carbon atoms.

21. The method of claim 20 wherein said alkanoic acid is a member selected from the group consisting of butyric acid, valeric acid, caproic acid, caprylic acid, capric acid, lauric acid, myristic acid, palmitic acid, stearic acid, and mixtures thereof.

22. The method of claim 16 wherein said heparin is a member selected from the group consisting of low molecular weight heparin, high molecular weight heparin, heparin fragments, recombinant heparin, heparin analogs, polysaccharides containing heparin activity, and mixtures thereof.

23. The method of claim 16 wherein said oil phase is a pharmaceutically acceptable oil.

24. A method for making a composition for obtaining enhanced mucosal absorption of heparin comprising:

(a) dissolving an amphiphilic heparin derivative comprising heparin covalently bonded to a hydrophobic agent selected from the group consisting of bile acids, sterols, alkanoic acids, and mixtures thereof in a pharmaceutically acceptable aqueous solvent such that said amphiphilic heparin derivative forms nanoparticles in said pharmaceutically acceptable aqueous solvent; and

(b) mixing a pharmaceutically acceptable surfactant with said nanoparticles in said pharmaceutically acceptable aqueous solvent and then disrupting said nanoparticles such that said

pharmaceutically acceptable surfactant interacts with the heparin and the hydrophobic agent, thereby exposing at least some of the hydrophobic agent on the outside of the nanoparticles.

25. The method of claim 24 wherein said hydrophobic agent is a bile acid selected from the group consisting of cholic acid, deoxycholic acid, chenodeoxycholic acid, lithocholic acid, ursocholic acid, ursodeoxycholic acid, isoursodeoxycholic acid, lagodeoxycholic acid, glycocholic acid, taurocholic acid, glycodeoxycholic acid, glycochenodeoxycholic acid, dehydrocholic acid, hyocholic acid, hyodeoxycholic acid, and mixtures thereof.

26. The method of claim 25 wherein said bile acid is deoxycholic acid.

27. The method of claim 24 wherein said hydrophobic agent is a sterol selected from the group consisting of cholestanol, coprostanol, cholesterol, epicholesterol, ergosterol, ergocalciferol, and mixtures thereof.

28. The method of claim 24 wherein said hydrophobic agent is an alkanoic acid comprising about 4 to 20 carbon atoms.

29. The method of claim 28 wherein said alkanoic acid is a member selected from the group consisting of butyric acid, valeric acid, caproic acid, caprylic acid, capric acid, lauric acid, myristic acid, palmitic acid, stearic acid, and mixtures thereof.

30. The method of claim 24 wherein said heparin is a member selected from the group consisting of low molecular weight heparin, high molecular weight heparin, heparin fragments, recombinant heparin, heparin analogs, polysaccharides containing heparin activity, and mixtures thereof.

31. The method of claim 24 wherein said pharmaceutically acceptable surfactant is a member selected from the group consisting of anion surfactants, cationic surfactants, amphoteric surfactants, anionic surfactants, amphiphilic surfactants, hydrophobic surfactants, and mixtures thereof.

32. The method of claim 31 wherein said pharmaceutically acceptable surfactant is a bile acid.

33. The method of claim 32 wherein said bile acid is deoxycholic acid.

34. A composition prepared according to the method of claim 1.

35. A composition prepared according to the method of claim 8.

36. A composition prepared according to the method of claim 16.

37. A composition prepared according to the method of claim 24.

38. A composition comprising a plurality of an amphiphilic heparin derivative comprising heparin covalently bonded to a hydrophobic agent selected from the group consisting of bile acids, sterols, alkanoic acids, and mixtures thereof, wherein said plurality of the amphiphilic heparin derivative is configured as a nanoparticle having an outer surface such that at least some of the hydrophobic agents are exposed on the outer surface.

39. A dosage form comprising a mixture of:

(a) an effective amount of a composition comprising a plurality of an amphiphilic heparin derivative comprising heparin covalently bonded to a hydrophobic agent selected from the group consisting of bile acids, sterols, alkanoic acids, and mixtures thereof, wherein said plurality of the amphiphilic heparin derivative is configured as a nanoparticle having an outer surface such that at least some of the hydrophobic agents are exposed on the outer surface; and

(b) a pharmaceutically acceptable carrier.

40. A method for treating a patient in need of anticoagulation therapy comprising administering an effective amount of a composition comprising a plurality of an amphiphilic heparin derivative comprising heparin covalently bonded to a hydrophobic agent selected from the group consisting of bile acids, sterols, alkanoic acids, and mixtures thereof, wherein said plurality of the amphiphilic heparin derivative is configured as a nanoparticle having an outer surface such that at least some of the hydrophobic agents are exposed on the outer surface.